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EVALUATION OF HPV INCIDENCE AND CERVICAL SMEAR RESULTS IN SYRIAN REFUGEES

SURİYELİ MÜLTECİLERDE HPV İNSİDANSI VE SERVİKAL SMEAR SONUÇLARININ DEĞERLENDİRİLMESİ

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Öz

Amaç: Çalışmamızın amacı, jinekoloji onkoloji polikliniğine başvuran Suriyeli kadınlarda HPV oranını saptamak, servikal patolojileri tespit etmektir.

Materyal ve Metot: Jinekoloji Onkoloji Polikliniği'ne Ocak 2014 ile Eylül 2018 tarihleri arasında başvuran 659 Suriyeli göçmen hasta çalışmaya dahil edildi. Gebe olanlar, histerektomi operasyonu geçirenler, HPV aşı öyküsü olanlar çalışma dışı bırakıldı. Hastaların demografik verileri [yaş, sosyoekonomik düzey, eğitim durumu, sigara alışkanlığı, parite, ilk ilişki yaşı, vücut kitle indeksi (BMI)] ve klinik bilgileri (servikal smear, HPV genotip ve servikal biyopsi sonuçları) değerlendirildi. Verilerin istatistiksel analizleri yapıldı. İstatistiki anlamlılık düzeyi $p<0,05$ olarak kabul edildi.

Bulgular: Çalışma süresi boyunca, kliniğimize çalışma kritelerimizi sağlayan toplam 659 Suriyeli kadın hasta başvurdu. Çalışmaya alınan Suriyeli göçmen hastaların yaş ortalamaları 25,13±4,20, %23,60'sının 18 yaş öncesi evlendikleri, %73,50'si lise ve üzeri öğrenim düzeyinde olduğu tespit edildi. Suriyeli göçmen kadınların (35/659) %5,30'unde HPV DNA pozitifliğine rastlandı. Çalışmamızda HPV 16 (8/35) %22,80; HPV 18 (6/35) %17,60; diğer yüksek riskli HPV tipleri %59,60 oranında görüldü. Hastaların (643/659) %97,60'ında smear sonucu normal; (9/659) %1,40'ında ASCUS; (2/659) %0,30'unda ASCH; (4/659) %0,60'ında LSIL; (1/659) %0,10'unda HSIL mevcuttu.

Sonuç: Suriyeli hastalarda bulunan HPV oranları ülkemizdeki kadınlara benzer orandaydı ve en sık bulunan tipler HPV 16 ve 18 dışındaki tiplerdi. Ülkemizde, Suriyeli göçmen kadınların daha uzun sürede kalacakları düşünüldüğünde zaten büyük sıkıntılar çeken bu hastalara daha etkin servikal kanser tarama programları yapılması ve aşılama hakkındaki bilgi eksikliklerini giderilmesi gerekmektedir.

Anahtar Kelimeler: Suriyeli hastalar, HPV, servikal smear, servikal biyopsi

Abstract

Objectives: The aim of this study was to determine the rate of HPV and cervical pathologies in Syrian women admitted to the gynecology-oncology outpatient clinic.

Materials and Methods: 659 Syrian refugee patients admitted to the gynecology oncology outpatient clinic between January 2014 and September 2018 were included in the study. Pregnant women, women who underwent a hysterectomy, and those with a history of HPV vaccine were excluded from the study. Demographic data [age, socioeconomic status, educational status, smoking habits, parity, age of first intercourse, body mass index (BMI)] and clinical information (cervical smear, HPV genotype and cervical biopsy results) of the patients were evaluated. The statistical significance level was accepted as $p<0.05$.

Results: During the study period, a total of 659 Syrian women who meet our study criteria admitted to our clinic. The mean age of Syrian patients included in the study was 25.13 ± 4.20 years, 23.60 % were married before the age of 18, and the educational status of 73.50% of patients were at high school and above. HPV DNA positivity was found in 5.30% (35/659) of the Syrian refugee women. In our study, HPV 16 was found in 22.80% (8/35); HPV 18 was positive in 17.60% (6/35); and other high-risk types were seen in 59.60% of patients. 97.60% of the patients (643/659) had normal smear results, while 1.40% (9/659) had ASCUS; 0.30% (2/659) had ASCH; 0.60% (4/659) had LSIL; and HSIL was present in 0.10% (1/659) of patients.

Conclusion: The rate of HPV in Syrian patients was similar to women in our country, and the most common (except HPV 16 and 18) are other types of high-risk HPV. Considering that the Syrian citizens will stay in our country for a longer period of time, more effective cervical cancer screening programs should be applied to the Syrian women who have already suffered from great difficulties and the information deficiencies about vaccination must be eliminated.

Keywords: Syrian patients, HPV, cervical smear, cervical biopsy.

Introduction

The ongoing civil war in Syria is one of the leading wars of our time. The civil war in Syria is completing its eighth year, and as a result of this crisis, Turkey is the country where most people emigrated refuge. According to records in 2019, Turkey is hosting more than 4 million Syrian refugees. That is about one-seventh of the population took refuge in Syria to Turkey.[1]

It is highly likely that migrants will have little to do with cancer prevention and vaccination programs and sexually transmitted diseases (STD) tests, resulting in costly treatments for treatment and survival in later years.[2] Health services for migrants should be provided without discrimination as a human right. After the migration waves, the primary level organization should be re-planned and the health services to be provided according to the changing population structure should be updated. Protective services for migrants should be provided on-site and refugees should not be expected to apply. Immigrants should be registered and necessary examinations and follow-up should be performed.[3] If registered, pregnant, infant, child, vaccine, and family planning follow-up will be performed and the requirements of preventive medicine will be fulfilled. The inadequacy of the conditions in the migrant groups or the negative approach to migrant groups triggers the emergence of many problems as well as public health problems.

Along with forced migration, the dynamics in the field of health in the migrated place begin to change. For a healthy society, screening programs for groups at risk for major diseases in migrants should be included in the services provided.[4] Determining the HPV prevalence of Syrian refugee women will be important for the planning of health care services to be provided to them. In particular, cervical cancer, which is one of the most important diseases affecting public health, needs to be addressed in these women. It is thought that infections caused by oncogenic HPV types are involved in the etiopathogenesis of almost all cervical cancers and precancerous lesions, and HPV types 16 and 18 may be responsible for approximately 70% of all cervical cancers.[5] The incidence of cervical cancer has increased in Turkey, and early diagnosis studies and national screening programs for free are rendered common in all sections of society, including the Syrian immigrant women. Informing Syrian migrant women about cervical cancer and HPV will facilitate integration in service delivery. We aim to focus on HPV which is one of the sexually transmitted diseases and is one of the health problems of Syrian refugees living in Turkey.

Materials and Methods

The study was conducted in the Oncology Center of Health Sciences University Tepecik Training and Research Hospital, which provides tertiary health care services and also provides basic health care services for patients through many health centers. Necessary permissions were obtained from the ethics committee (January

10,2018/65- Health Sciences University Tepecik Training and Research Hospital) and Republic of Turkey of Directorate Interior General of Migration of Management for the study (Izmir Migration Administration 02.07.2019/E35437). In this study, we evaluated smear, HPV genotype and cervical biopsy results of 659 Syrian migrant patients admitted between January 2014 and September 2018. The records of the patients at all stages from the time of admission to treatment are adequately and regularly recorded, and the treatments applied are written in detail. There is an appropriate registration and coding system in terms of statistics and evaluation of health care. In order to prevent communication problems with Syrian patients in our hospital, translators have the necessary knowledge and experience and work according to the principle of confidentiality and impartiality. The examinations were conducted with the help of an interpreter. Age, socioeconomic status, educational status, smoking habit, parity, age at first intercourse, and body mass index (BMI) were recorded. Cases with insufficient biopsy and/or no biopsy were excluded from the study.

Each woman who participated in the study gave two samples, one for liquid-based cytology test (Collection Vial 10 ml, BD Sure Path, USA) and the other for HPV DNA testing. First, cervical specimens were selected from patients who were not in the menstruation period, did not undergo vaginal treatment for the last three days, vaginal acetic acid and lugol solution was not applied before the test and did not have sexual activity within 24 hours. Cytology test results were obtained based on the 2001 Bethesda classification in the Pathology laboratory of our hospital. Swab samples were taken from the patients by using Female Swab Specimen Collection Kit (HybriBio, HongKong) for the detection of cervical HPV DNA during the examination and brought to the Microbiology Laboratory of our hospital. HPV-DNA testing was performed using the real-time polymerase chain reaction method (Cobas® 4800 HPV Amplification / Detection Kit, Roche Diagnostics, USA). Samples found positive were identified as HPV-16, HPV-18 and other high risk HPV (types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68).[6]

In our oncology center, all patients underwent colposcopic examination by experienced colposcopists. Colposcopic examinations were performed with a binocular colposcope (Colposcope 1D-21100, Leisegang GmbH, 2014-03, Germany) with a green filter capable of 4.5 to 30 magnifications. Cervical biopsy was performed with forceps from the areas where acetowhite, mosaic, punctuation, leukoplakia, atypical vascularity was observed and iodine-free. The patients who had pathological colposcopic findings were treated in our center for treatment and / or requiring further treatment. Cervical biopsy specimens were sent to the pathology unit in formaldehyde for evaluation. Diagnoses obtained from histological samples were taken as the gold standard. If the findings analyzed by histology were more serious, the later procedures were accepted as a definitive diagnosis. The cases with normal histological samples were taken as negative results.

Statistical analysis

Statistical analysis of the data was performed by SPSS (Version 22.0, SPSS Inc., Chicago, IL, USA) package program. Descriptive statistics were presented as mean ± standard deviation and median (min-max) for continuous variables, and as numbers and percentages for categorical data. The distribution of normality of data for statistical test selection was evaluated by Kolmogorov-Smirnov and Shapiro-Wilk tests. The t-test was used to compare the age of the patients according to the HPV groups. The correlation studies between categorical variables and ratio comparisons were performed with the Chi-square test or Fisher's exact test. Statistical significance level was accepted as $p < 0.05$.

Results

Our study was conducted with 659 women who migrated from Syria. The mean age, educational status, financial status, contraception method, parity, sexual activity time, smoking were presented in Table 1. HPV positivity of the cases were presented in Table 2 and no statistically significant difference was found (p=0.690;p=0.212; p=0.238;p=0.445;. p=0.328; p=0.742 and p=0123, respectively). 70.60% of women stated that they used withdrawal method to prevent pregnancy. 23.60% of the women in the study group were married before the age of 18, 73.50% were at high school level and above, and stated that going to school delayed the marriage age. It was found that most of the female refugees (80.50%) did not speak Turkish and 90.70% of them were under $ 500 in income (Table 1).

When the demographic data and the presence of the hr-HPV genotype were compared statistically, no statistical significance was found (Table 2). Carcinogenic high-risk (16, 18), and other high-risk (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68) HPV genotype was investigated in our study, HPV DNA positivity was found in 5.30% (35/659) of Syrian women. hr-HPV positivity was detected in 4.50% (29/645) of the patients with normal cervical cytology and found in 37.50% (6/16) of the patients with abnormal cervical cytology. HPV-16 positivity was found in 22.80% (8/35), HPV-18 was found in 17.60% (6/35) and other high-risk types were seen in 59.60% of patients (Table3).

Smear results were normal in 97.60% of patients (643/659). ASCUS was reported in 1.40% (9 of 659), ASCH in 0.30% (2 of 659), LSIL in 0.60% (4 of 659), and HSIL was reported in 0.10% (1 of 659) of patients. According to the smear results, smear and HPV negative patients were 96.20% (614/643), whereas smear negative and HPV positive patients were 4.50% (16/649).

In our practice, if ASCUS is the result of cervical cytology at 3 months follow-up in ASCUS cases, cervical biopsy is routinely performed in ASCH cases and other high risk HPV genotype cases such as HPV 16, HPV 18. Cervical

biopsy result of 1 patient with HSIL cervical cytology reported as LSIL; whereas 4 of cervical biopsy of 5 LSIL patients were reported as LSIL, 1 of them reported as normal. Cervical biopsy was reported as normal in 8 of 9 patients with ASCUS, whereas 1 of them has LSIL. One of the 2 ASCH cervical cytology patients had LSIL and the other had normal biopsy results. The remaining 29 HPV positive patients had normal cervical biopsy results (Table 2). In patients who underwent biopsy, control cervical cytology was performed three months and six months after the procedure. All control smears of the patients who underwent biopsy until the completion of our study were evaluated as normal.

Discussion

Cervical cancer is the second most common type of cancer among women in the world and is the second most common cause of cancer-related deaths in women.[7] It is responsible for approximately 10% of all cancer deaths.[8] Epidemiological studies supported by molecular technology have proven the main role of HPV infections in the development of cervical cancer. The most carcinogenic HPV genotype is HPV type 16 and is responsible for 55-60% of all cervical cancers. HPV genotype 18 comes second and accounts for 10-15% of cervical cancers.[9]

Data on the prevalence of HPV in a population are influenced by vaccination, treatment strategies, and external migration. In this study, HPV positivity was found in 5.40% of women during routine cervical cancer screening. This positivity rates in Syrian migrant women, with 37.50% in women with abnormal cervical cytology is similar to the prevalence of HPV infection in Turkey.[10] Several studies have been conducted to evaluate the HPV genotype distribution in Turkey.[9,11] According to these studies, HPV prevalence rates vary from 4.90% to 57.50%. Our study is hospital-based, and to our knowledge, it is the first study conducted in the Syrian immigrant women and therefore, There is a need for future, large-scale studies including data from community health centers and other hospitals for precise information on the HPV type distribution in Turkey. In a study conducted among Latin American women, HPV incidence was 14.50% to 16.60% in women with normal cervical cytology.[12,13] The risk of HPV 16/18 among women in neighboring countries is different in the literature. However, we can say that the incidence of HPV decreases as we move towards eastern societies. The incidence of HPV among Georgia, Russia, Greece, Bulgaria and Iran is 1.1%, 9.4%, 2.8%, 9.7% and 2.8%, respectively.[14-18]

In our study, other types than hr-HPV 16-18 were more common than the sum of HPV 16 and 18. According to the study performed in women with normal cervical cytology in Turkey, the cumulative rate of HPV types other than type 16 or type 18 is more common as shown in our study.[9,11] Similarly, in studies in the Egypt and Kingdom of Bahrain, hrHPV types other than type 16 and type 18 were more common.[19,20]

Table 1. Clinical characteristics of study population (n=659)

	Mean ± SD	**Median (min-max)**
Age (years)	25.13 ± 4.20	25 (19-36)
Age at first intercourse	19.24 ± 3.46	21 (16-29)
BMI	23.22 ± 3.04	23 (19.2-30.5)
Gravida	4.32 ± 1.21	4 (0-7)
Parity	3.12 ± 0.93	3 (0-6)
Abortion	0.25 ± 0.48	0 (0-3)
	n	**%**
Smoking Status		
Smoker	45	6.80
Non-smoker	614	93.20
Contraception		
Withdrawal	465	70.60
OCPs	26	3.90
IUD Others	44 124	6.60 18.90
Education		
Primary school	159	24.20
Secondary and high school	485	73.50
University	15	2.30
Intercourse before age of 18		
Yes	156	23.67
No	503	76.33
Language		
Yes	128	19.50
No	531	80.50
Income		
500 $	598	90.70
500-1000 $	44	6.60
> 1000 $	17	2.70

Data are presented as mean ± standard deviation, SD: standard deviation, min: minimum, max: maximum.
BMI : Body mass index (kg/m2),OCP: oral contraceptive pills, IUD: intrauterin device

Table 2. Demographic data and evaluation of HPV type

		HPV		P
		Negative	Positive	
School	primary school	152	7	0.212
	Secondary and high school	460	25	
	University	12	3	
Income	500 $	567	31	0.238
	500-1000 $	41	3	
	> 1000 $	16	1	
Contraception	Withdrawal	441	24	0.445
	OCPs	24	2	
	IUD	41	3	
	others	118	6	
Parity	0	86	5	0.328
	1	134	9	
	>1	404	21	
Intercourse before age of 18	Yes	144	12	0.742
	No	480	23	
Age		25.48 ± 3.90	24.86 ± 4.10	0.690
Smoking conditions	Smoker	39	6	0.123
	Non-smoker	585	29	

Student t test, Fisher exact test and Chi-square test were used.
HPV: Human Papilloma Virus.

Table 3. Comparison of HPV negative and HPV positive cases.

	No HPV	hr-HPV	Other hr-HPV
Normal (643)	614	11	18
ASCUS (9)	8	-	1
ASCH (2)	2	-	-
LSIL (4)		2	2
HSIL (1)	-	1	-

*HPV 16, 18, and other high risk HPV types (31, 33,35, 39, 45,51, 52, 56, 58, 59, 66, and 68)
HPV, Human Papilloma Virus; ASCUS , atypical squamous cells of undetermined significance; ASC-H, atypical squamous cells when high-grade intraepithelial lesions (ASC-H) cannot be ruled out; HSIL, high-grade squamous intra-epithelial lesions; LSIL,histopathological low-grade squamous intraepithelial lesion ; hr-HPV, High-risk HPV types (oncogenic or cancer-associated); other hr-HPV, Low-risk HPV types (nononcogenic or noncancer-associated)

HPV types 16 and 18 have been commonly described in the majority of cases of cervical cancer, but the contribution of HPV type 16 and HPV type 18 to cervical cancer is substantially lower in cytologically normal women.[13-19] In our study, all cervical biopsies performed to hr-HPV positive patients with normal cervical cytology were found as normal. The prevalence of HPV is highest in women under the age of 35 and generally decreases in older age in many populations.[21] However, in our study, there was no significant difference in the prevalence of HPV by age. Similar studies also showed no difference.

As seen in our study, Syrian women have a high fertility rate. It has been shown in many studies that the availability and quality of maternal and child health, family planning, and preventive services for migrant women have a positive effect on the regulation of their fertility.[22,23] The age at first marriage is an important demographic indicator in terms of determining the level of exposure of women to STD related risks. Populations where the first marriage age is small tend to be populations with early childbearing and high fertility. According to the data of 2014 in Syria, 13.3% of girls got married before the age of 18 and the fertility rate in the 15-19 age group is 40.02%.[23,24] As can be seen in our study, Syrian refugee women have same reproductive abilities while in Turkey. Although legal marriage age is 17 in Syria, exceptions can be made with the permission of religious leaders.[23,24] In our study, the fact that there are many pregnancies under the age of 18, and that the girls in Syria started to marry from the age of 15, and that these marriages are mostly approved by the state authorities reflects the Syrian society's view of early age marriages.[25,26]

Household income is also one of the important factors affecting STD. STD level and perception are influenced by the culture, values, beliefs, right of the woman to control her own body, traditions, monogamy or polygamy.[22,27]

Our contributions to the literature: Refugees are experiencing serious health problems in the countries they migrate to, and they cause serious health problems in the communities they migrate. We believe that this study is important because there is no study in sexually transmitted diseases which is specific to refugees in Turkey. Addressing the problems created by the migrants coming to our country in health services is important in terms of contributing to scientific data. In this study, the prevalence of HPV in Syrian refugees in Turkey has been found at a similar rate to Turkish society. However, due to lack of information on the services provided, it has been shown that it may pose risks to public health. Inadequate information and guidance on cervical cancer, HPV vaccines and cervical cytology screenings may cause problems in terms of public health as well as in the future, if not for the present. Providing social projects for the screening and treatment of sexually transmitted diseases of Syrian refugee women facing health risks and health and social workers providing preventive and therapeutic health services will further facilitate the state's financial burden. The fact that our study was conducted in a single center constitutes the limitation of the study, but the fact that the health services in the

region are similar to the other regions of the country and the homogeneous distribution character of the refugees suggest that the results are important in terms of contribution to the literature.

As a result, HPV prevalence data in Syrian migrant women should be considered in the decision to participate in vaccination and screening programs like other members of the society. For this purpose, studies should be done for broad-based participation in Turkey. Although HPV type 16 is known to be the most common type worldwide, our results have shown that hrHPV types other than type 16 or type 18 are the most common genotypes in women undergoing routine cervical cancer screening. Therefore, detection of other HPV species is important for screening cervical cancer. In addition, identification of HPV types in Syrian migrant women through multicenter studies is important for determining the prevalence of HPV genotype and monitoring.

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